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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/756,767	01/14/2004	Motoki Kyo	032084	1737

38834 7590 12/20/2007

WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP
1250 CONNECTICUT AVENUE, NW
SUITE 700
WASHINGTON, DC 20036

EXAMINER	
CROW, ROBERT THOMAS	
ART UNIT	**PAPER NUMBER**
1634	

MAIL DATE	DELIVERY MODE
12/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/756,767	KYO ET AL.	
	Examiner	Art Unit	
	Robert T. Crow	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,20-27,29,30-31 and 33-42* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 34-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,20-27,29-31 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 3 October 2007 in which claims 17, 20-21, 23, and 25 were amended, no claims were canceled, and no new claims were added. All of the amendments have been thoroughly reviewed and entered.

The interview summary is acknowledged and the interview record is complete.

The objections to the specification listed in the previous Office Action withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 112, second paragraph, are withdrawn in view of the amendments.

The previous rejections under 35 U.S.C. 103(a) not reiterated below are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed and are addressed following the rejections necessitated by the amendments.

Claims 17, 20-27, 29, 30-31, and 33 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. The following rejections under 35 USC 112, second paragraph, are new rejections necessitated by the amendments.

4. Claims 17, 20-22, 24-27, 39, 30-31, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17, 20-22, 24-27, 39, 30-31, and 33 are indefinite in claims 17 and 21, which recite the limitation "expressed by -(O-R1)n" in line 21 of claim 17 and in line 12 of claim 21 because neither claim defines "n." It is suggested that the claims be amended to indicate what "n" represents.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. The following rejections are new rejections necessitated by the amendments.

8. Claims 17, 21-24, 26-27, and 29-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Corn et al (U.S. Patent No. 6,127,129, issued 3 October 2000) in view of Fodor et al (U.S. Patent No. 5,424,186, issued 13 June 1995) as evidenced by Sato et al (U.S. Patent No. 5,997,958, issued 7 December 1999).

Regarding claim 17, Corn et al teach a biomolecule interaction measuring method. In a single exemplary embodiment, Corn et al teach providing a double-stranded oligonucleotide array comprising a background region on which a hydrophilic polymer molecule is immobilized and a region on which a plurality of double-stranded oligonucleotides are immobilized on a metal substrate; namely, Figure 1, wherein PEG is the hydrophilic polymer (column 10, lines 27-28) on the background region, the substrate is gold, and the attached DNA is double stranded (column 12, Example 1). Corn et al further teach measuring the interaction between said double-stranded oligonucleotides and a biomolecule or aggregate thereof; namely, SPR (i.e., surface plasmon resonance) imaging measurements are taken of the binding of single-stranded DNA binding protein to an array of double-stranded DNA sequences (figure 5 and Example 1). Corn et al further teach each of said double-stranded oligonucleotide include a first single-stranded oligonucleotide and a second single-stranded oligonucleotide, said first and second single-stranded oligonucleotides being entirely or partially bonded together in a complementary manner to form said double-stranded oligonucleotide; namely, the array has double stranded DNA sequences (Example 1). Corn et al also teach only said first single-stranded oligonucleotide is bonded to said substrate; namely, Figure 5, wherein the double-stranded DNA is prepared by immobilizing an oligonucleotide (e.g., D2) and hybridizing the complement to the sequence (column 13, lines 7-28).

Corn et al also teach the first single stranded oligonucleotide is bonded to said substrate by use of a heterobifunctional polymer molecule in the form of the hydrophilic polymer MUAM (column 7, lines 53-54), which has a mercapto group covalently bound to a surface of a solid surface (i.e., X; column 3, lines 58-59) and an amino group (i.e., Y) which attaches to the DNA (step 5 of Figure 4). Corn et al do not teach a hydrophilic repeating unit (expressed by -(O-R1)n, wherein R1 is an alkylene group of the polymer (i.e., polyethylene glycol, or PEG). Thus, Corn et al teach a base method that differs from the instantly claimed method because Corn et al does not teach the a heterobifunctional linker wherein the X group and the Y group are linked with a polyethylene glycol portion.

However, Fodor et al teach an array of oligonucleotides immobilized in an array on a surface of a substrate (Abstract), wherein the oligonucleotide is immobilized using a heterobifunctional linker having a functional group X in the form of an amine and a functional group Y in the form of a carboxyl group which is derived from photocleavage of the molecule NVOC, and a hydrophilic repeating polymer in the form of ethylene glycol oligomers (column 14, lines 28-45 and column 3, line 52-column 4, lines 5). The substrate is metal (Example 1). Fodor et al also teach the linker comprising the NVOC group has the added advantage of allowing the use of lithographic techniques for synthesizing the oligonucleotide polymers on relatively small and precisely known locations on the substrate (column 2, lines 60-67). Thus, Fodor et al teach the known technique of using polyethylene glycol linkers in nucleic acid arrays.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising heterobifunctional linkers as taught by Corn et al by substituting the specific heterobifunctional linker comprising an amino group which attaches to a substrate and is attached to a polyethylene glycol linker, which is attached to a carboxyl group for attaching to the nucleic acid, as taught by Fodor et al with a reasonable expectation of success. Sato et al teach that amino groups have a strong affinity for gold (column 5, lines 20-25). Thus, the amino group on the linker of Fodor et al binds to the gold substrate of Corn et al. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added advantage of allowing the use of lithographic techniques for synthesizing the first single-stranded oligonucleotide polymers on relatively small and precisely known locations on the substrate as explicitly taught by Fodor et al (column 2, lines 60-67). In addition, it would have been obvious to the ordinary artisan that the known technique of using the polyethylene glycol based linkers of Fodor et al could have been applied to the substrate of Corn et al with predictable results because the linkers of Fodor et al predictably result in linkers suitable for attaching oligonucleotides to metal substrates.

Regarding claims 21-24, 26-27, and 29-30, Corn et al teach a biomolecule interaction measuring method. In a single exemplary embodiment, Corn et al teach measuring the interaction between a first biomolecule and a second biomolecule or an aggregate thereof in the form of taking SPR (i.e., surface plasmon resonance) imaging measurements of the binding of single-stranded DNA binding protein to an array of single-stranded and double-stranded DNA sequences (i.e., claim 27; Figure 5 and Example 1). Corn et al also teach use of a solid substrate with a solid surface comprising a background region on which a hydrophilic polymer molecule is immobilized other than the area; namely, Figure 1, wherein PEG is the hydrophilic polymer (column 10, lines 27-28) on the background region, and the PEG is not on the other areas of the substrate. The substrate also has a region on which said first biomolecule is immobilized; namely, DNA is immobilized on areas other than those where the PEG is immobilized (Figure 1).

Corn et al further teach the method wherein said substrate includes plural kinds of first biomolecules arranged thereon in an array arrangement; namely, Figure 1 and Example 1, wherein Example 1 has two different DNA sequences immobilized on a checkerboard surface (i.e., claim 26; column 12, lines 45-55).

Corn et al also teach the method wherein the interaction between said first biomolecule and said second biomolecule or aggregate thereof is measured through surface plasmon resonance imaging (i.e., claim 29; Figure 6; column 5, lines 40-50), and wherein said second biomolecule is a protein; namely, single-stranded DNA binding protein (i.e., claim 30; Example 1).

Corn et al also teach the first single stranded oligonucleotide is bonded to said substrate by use of a heterobifunctional polymer molecule in the form of the hydrophilic polymer MUAM (column 7, lines 53-54), which has a mercapto group covalently bound to a surface of a solid surface (i.e., X; column 3, lines 58-59) and an amino group (i.e., Y; claim 24) which attaches to the DNA (step 5 of Figure 4). Corn et al do not teach a hydrophilic repeating unit (expressed by -(O-R1)n, wherein R1 is an alkylene group of the polymer (i.e., polyethylene glycol, or PEG). Thus, Corn et al teach a base method that differs from the

instantly claimed method because Corn et al does not teach the a heterobifunctional linker wherein the X group and the Y group are linked with a polyethylene glycol portion.

However, Fodor et al teach an array of oligonucleotides immobilized in an array on a surface of a substrate (Abstract), wherein the oligonucleotide is immobilized using a heterobifunctional linker having a functional group X in the form of an amine and a functional group Y in the form of a carboxyl group (i.e., claim 24) which is derived from photocleavage of the molecule NVOC, and a hydrophilic repeating polymer in the form of ethylene glycol oligomers made up of 2-10 monomers (i.e., claim 23; column 14, lines 28-45 and column 3, line 52-column 4, lines 5). The heterobifunctional polymer has a molecular weight of 200 to 2000 (i.e., claim 22). The substrate is metal (Example 1). Fodor et al also teach the linker comprising the NVOC group has the added advantage of allowing the use of lithographic techniques for synthesizing the oligonucleotide polymers on relatively small and precisely known locations on the substrate (column 2, lines 60-67). Thus, Fodor et al teach the known technique of using polyethylene glycol linkers in nucleic acid arrays.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising heterobifunctional linkers as taught by Corn et al by substituting the specific heterobifunctional linker comprising an amino group which attaches to a substrate and is attached to a polyethylene glycol linker, which is attached to a carboxyl group for attaching to the nucleic acid, as taught by Fodor et al with a reasonable expectation of success. Sato et al teach that amino groups have a strong affinity for gold (column 5, lines 20-25). Thus, the amino group on the linker of Fodor et al binds to the gold substrate of Corn et al. The modification would result in a linker having a molecular weight of 200 to 2000 (i.e., claim 22), an n value of 2-10 ethylene glycol units (i.e., claims 21 and 23), and amino and carboxyl groups as X and Y, respectively (i.e., claims 21 and 24). The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added advantage of allowing the use of lithographic techniques for synthesizing the first single-stranded oligonucleotide polymers on relatively

small and precisely known locations on the substrate as explicitly taught by Fodor et al (column 2, lines 60-67). In addition, it would have been obvious to the ordinary artisan that the known technique of using the polyethylene glycol based linkers of Fodor et al could have been applied to the substrate of Corn et al with predictable results because the linkers of Fodor et al predictably result in linkers suitable for attaching oligonucleotides to metal substrates.

Response to Arguments

Applicant's arguments filed 16 July 2007 (i.e., the "Remarks") have been fully considered but they are not persuasive for the reason(s) listed below.

A. It is noted that the document of Kyo et al is listed on the "Notice of References Cited" form PTO-892 included with this Office Action because the reference was submitted with the Remarks but not listed on an Information Disclosure Statement.

B. Applicant argues on page 13 of the Remarks that in the interview of 12 June 2007, the examiner clarified that Fodor et al was relied upon for a linker to replace the entire linker of Corn et al.

Applicant is correct that the examiner is replacing the entire SSMCC linker of Corn et al with the hydrophilic linker of Fodor et al.

C. Applicant provides a table on page 14 or the Remarks summarizing the linkers of the claimed invention, Corn et al, and Fodor et al.

However, the Table provided by Applicant has several inaccuracies.

I. The first inaccuracy is that the heterobifunctionalilty of the linker of Fodor et al is not disclosed. The linker is, in fact, heterobifunctional because the linker has a functional group X in the form of an amine and a functional group Y in the form of a carboxyl group which is derived from photocleavage of the molecule NVOC, and a hydrophilic repeating polymer in the form of ethylene glycol oligomers (column 14, lines 28-45 and column 3, line 52-column 4, lines 5). Thus, because the linker has two different functional groups at each end, the linker is heterobifunctional.

II. The second inaccuracy is that the X group bound to the solid surface is not disclosed. Fodor et al specifically teach a combination of ethylene glycol with an amino group at the end for attachment to the substrate (column 14, lines 28-46). Thus, Fodor et al explicitly teach the functional group attached to the substrate.

III. The third inaccuracy s that the functional group bound to the oligonucleotide is not disclosed. The carboxyl group derived from photocleavage of the NVOC molecule on the linker is the group that is bound to the oligonucleotide chain. Thus, the functional group bound to the nucleic acid is disclosed.

IV. The fourth inaccuracy is that Fodor only teach glass substrates. Fodor et al also teach the surface of the substrate is metal (Example 1).

D. Applicant argues on pages 14-15 of the Remarks that the reference of Kyo et al shows "a robust increase of SPR signal" using NHS-PEG-MAL as opposed to SSMCC, thereby providing optimal (i.e., unexpected) results.

However, the results presented in the reference of Kyo et al are not commensurate in scope with the instant claims. The linker of Kyo et al is specifically a succinimide-PEG-maleimide linker of molecular weight 3400 (page 156). Neither of independent claims 17 or 21 requires this specific linker. In addition, dependent claim 22 allows a much broader range of molecular weight (i.e., 200 to 20000), dependent claim 23 allows a large range in the number of ethylene glycol units outside of the number encompassed by the linker of the Kyo et al reference, and dependent claim 24 encompasses functional groups other than the succinimide group and maleimide group of the linker of Kyo et al reference.

In addition, the reference of Kyo et al compares a succinimide-PEG-maleimide linker with the linker SSMCC (page 156). Corn et al teach a linker comprising a MUAM molecule covalently linked to SSMCC (Figure 1); thus, experiment reported by Kyo et al does not compare the succinimide-PEG-maleimide linker having the alleged unexpected results with the actual linker used by Corn et al.

Therefore, the linker having the alleged unexpected results is not commensurate in scope with the instant claims. See MPEP 716.02(d)[R-2].

D. Applicant argues on page 15 of the Remarks that the substitution of the linker of Fodor for the linker of Corn et al is fatal to the combination of Corn et al with Fodor et al because one is hydrophobic and the other is hydrophilic.

However, this argument is confusing because Applicant provides no evidence of the "fatality" of the combination. Corn et al teach the **background** must be hydrophobic to allow for pinning of solutions at specific locations (i.e., the nucleic acid spots; column 3, lines 15-42). Thus, Corn actually requires the areas **not** attached to nucleic acids to by hydrophobic, which, in turn, requires the areas that **do** have the nucleic acids to be hydrophilic. Thus, Corn et al clearly suggest that regions to which nucleic acids will be attached should not be hydrophilic, and are, therefore, hydrophilic. The background region is converted to a hydrophilic area **after** attachment of nucleic acids (Figure 1). Thus, the combination is not "fatal."

In addition, as evidenced by the prior art of Drumheller, background regions of hydrophilic polymers and attachment areas that are also hydrophilic are entirely compatible (see the rejection of claim 25 in Section 9 below and Drumheller, U.S. Patent No. 6,874,165, issued 23 February 1999, columns 1, 5, and 10-15).

E. Applicant argues there is no motivation to modify the linker of Corn et al with another linker.

However, as detailed in the rejections above, Fodor et al also teach the linker has the added advantage of allowing the use of lithographic techniques for synthesizing the oligonucleotide polymers on relatively small and precisely known locations on the substrate (column 2, lines 60-67). Thus, Fodor et al teach the known technique of using polyethylene glycol linkers in nucleic acid arrays.

It would therefore have been obvious to a person of ordinary skill in the art at the time the claimed invention was made to have modified the method comprising heterobifunctional linkers as

taught by Corn et al by substituting the specific heterobifunctional linker comprising an amino group which attaches to a substrate and is attached to a polyethylene glycol linker, which is attached to a carboxyl group for attaching to the nucleic acid, as taught by Fodor et al with a reasonable expectation of success. Sato et al teach that amino groups have a strong affinity for gold (column 5, lines 20-25). Thus, the amino group on the linker of Fodor et al binds to the gold substrate of Corn et al. The ordinary artisan would have been motivated to make such a modification because said modification would have resulted in a method having the added advantage of allowing the use of lithographic techniques for synthesizing the first single-stranded oligonucleotide polymers on relatively small and precisely known locations on the substrate as explicitly taught by Fodor et al (column 2, lines 60-67). In addition, it would have been obvious to the ordinary artisan that the known technique of using the polyethylene glycol based linkers of Fodor et al could have been applied to the substrate of Corn et al with predictable results because the linkers of Fodor et al predictably result in linkers suitable for attaching oligonucleotides to metal substrates.

In addition, it is also noted that under the Supreme Court ruling for *KSR Int'l Co. v. Teleflex, Inc* (No 04-1350 (US 30 April 2007) forecloses the argument that a **specific** teaching suggestion, or motivation is required to support a finding of obviousness. See *Ex parte Smith* (USPQ2d, slip op. at 20 (Bd. Pat. App. & Interf. June 25, 2007).

F. Applicant also argues on page 15 of the Remarks that Fodor et al do not teach immobilization to a gold layer, as required for SPR.

However, Fodor et al is not relied upon for attachment to a thin gold layer; rather, attachment of the linker to a gold layer, as well as SPR, is taught by Corn et al as detailed above.

In addition, claims 17 and 20-24 do not require a thin gold layer; rather, claims 17 and 20 merely require a metal substrate and claims 21--24 only require a substrate with a solid surface.

Furthermore, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

9. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Corn et al (U.S. Patent No. 6,127,129, issued 3 October 2000) in view of Fodor et al (U.S. Patent No. 5,424,186, issued 13 June 1995) as evidenced by Sato et al (U.S. Patent No. 5,997,958, issued 7 December 1999) as applied to claim 21 above, and further in view of Drumheller (U.S. Patent No. 6,874,165, issued 23 February 1999).

Regarding claim 25, the method of claim 21 is discussed above in Section 8.

While Corn et al also teach the method wherein the solid surface comprises a thin gold layer formed on said surface (column 3, line 53-column 4, line 8), neither Corn et al nor Fodor et al teach a compound with the formula X'-R'-Y' is between the gold layer (i.e., the substrate) and the other heterobifunctional hydrophilic polymer.

However, Drumheller et al teach a biochip in the form of a gold support (column 11, lines 30-45), having bioactive species in the form of nucleic acids, which are oligonucleotides, immobilized thereon Abstract and column 1, lines 15-40). The immobilized oligonucleotides are on a linker that is a second layer on top of a first layer of linkers on the gold substrate (Abstract). The first linker is a polyethylene glycol molecule, which is an organic group R' (column 11, line 45-column 12, line 16), and which has two functional groups (column 10, line 60-column 11, line 14). The functional groups include mercapto (i.e., thiol) and amino (i.e., amine; column 15, lines 15-40). Drumheller et al also teach the second layer having the attached oligonucleotides is also a polyethlyene glycol (column 14, lines 50-65) having similar ends (column 15, lines 15-40). Drumheller et al also teach the arrangement of linkers has the added advantage of increasing the hydrophilicity of the substrate, which facilitates the immobilization of the oligonucleotide (i.e., bioactive species; column 5, lines 1-12). Thus, Drumheller teaches the known technique of using a gold surface with a polymer X'-R'-Y' on the surface that in turn is attached to a second polymer X-R-Y.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the method comprising a gold film with a first polymer X-R-Y as taught by Corn et al in view of Fodor et al with the additional polymer X'-R'-Y' between the gold surface and the first polymer as taught by Drumheller with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in a method having the added advantage of increasing the hydrophilicity of the substrate, which facilitates the immobilization of the oligonucleotide as explicitly taught by Drumheller (column 5, lines 1-12). In addition, it would have been obvious to the ordinary artisan that the known technique of using the additional polymer X'-R'-Y' on the gold surface of Drumheller could have been applied to the substrate of Corn et al in view of Fodor et al with predictable results because the additional polymer X'-R'-Y' on the gold surface of Drumheller predictably results in a surface useful for immobilizing nucleic acids.

10. Claims 20 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Corn et al (U.S. Patent No. 6,127,129, issued 3 October 2000) in view of Fodor et al (U.S. Patent No. 5,424,186, issued 13 June 1995) as evidenced by Sato et al (U.S. Patent No. 5,997,958, issued 7 December 1999) as applied to claims 17 and 30 above, and further in view of Noblett (U.S. Patent No. 6,362,004 B1, issued 26 March 2002).

Regarding claims 20 and 33, the method of claim 17 and 30 are discussed above in Section 8.

Neither Corn et al nor Fodor et al teach markers on the array indicative of spots. Thus, Corn et al in view of Fodor et al teach a base method that differs from the instantly claimed method because Corn et al in view of Fodor et al does not teach markers on the array indicative of spots.

However, Noblett et al teach the use of microarrays comprising immobilized nucleic acids (column 1, lines 20-30) having marks indicative of spots (i.e., fiducials, Abstract) with the added advantage of allowing positioning and alignment of the substrate for spot analysis and comparison

procedures (Abstract). Thus, Noblett teaches the known technique of using markers on the array indicative of spots.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to have modified the method as taught by Corn et al in view of Fodor et al with the fiducials as taught by Noblett with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in a method having the added advantage of allowing positioning and alignment of the substrate for spot analysis and comparison procedures as explicitly taught by Noblett (Abstract). In addition, it would have been obvious to the ordinary artisan that the known technique of using the markers of Noblett could have been applied to the substrate of Corn et al in view of Fodor et al with predictable results because the markers of Noblett predictably result in indicators of spots suitable for use with nucleic acid arrays.

11. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Corn et al (U.S. Patent No. 6,127,129, issued 3 October 2000) in view of Fodor et al (U.S. Patent No. 5,424,186, issued 13 June 1995) as evidenced by Sato et al (U.S. Patent No. 5,997,958, issued 7 December 1999) as applied to claim 30 above, and further in view in view of Wiegel (U.S. Patent No. 6,107,034, issued 22 August 2000).

Regarding claim 31, the method of claim 30 is discussed above in Section 8.

Corn et al do not teach markers indicative of spots. While Corn et al also teach the second biomolecule is a protein in the form of single-stranded DNA binding protein (Example 1), Corn et al do not specifically teach transfer factors. Thus, Corn et al in view of Fodor et al teach a base method that differs from the instantly claimed method because Corn et al in view of Fodor et al does not teach transfer factors.

However, Wiegel teaches the detection of binding of a transfer factor to nucleic acids (e.g., GATA-3 binding to the DNA motif recognized by the protein; column 3, lines 52-63) and the use of nucleic acid arrays (column 6, lines 3-14) with the added benefit that detection of the transfer factor

GATA-3 provides a diagnostic test for a hormone responsive tumor (Abstract). Thus, Wiegel teaches the known technique of using transfer factors.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the method comprising detection of protein binding as taught by Corn et al in view of Fodor et al with the transfer factor protein GATA as taught by Wiegel et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in a method having the added advantage of providing a diagnostic test for a hormone responsive tumor as explicitly taught by Wiegel (Abstract). In addition, it would have been obvious to the ordinary artisan that the known technique of using the transfer factors of Wiegel could have been applied to the substrate of Corn et al in view of Fodor et al with predictable results because the transfer factors of Wiegel predictably bind to nucleic acids.

Response to Arguments

Applicant's remaining arguments rely on arguments set forth to address the alleged deficiencies of Corn et al in view of Fodor et al. These arguments are addressed above in Section 8. Since these arguments were not persuasive, the rejections of the remaining claims are maintained.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

14. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571) 272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jehanne Sitton/
Primary Examiner
12/18/2007

Robert T. Crow
Examiner
Art Unit 1634